

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Art Unit: To be assigned

Application No.: To be assigned

Filed: Herewith

For: METHODS FOR TREATING CELLS

Examiner: To be assigned

Date: June 6, 2001

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BOX PATENT APPLICATION  
COMMISSIONER FOR PATENTS  
WASHINGTON, D.C. 20231

**PRELIMINARY AMENDMENT**

Prior to examining the above-identified application, please amend the specification as follows:

**In the specification:**

On page 1, line 2, please insert the following paragraph:

**--Priority Claim**

This application claims priority under 35 U.S.C. § 119 to Great Britain Application No. 0013817.2, filed June 6, 2000.--

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On page 2, line 21, please delete the paragraph that reads:

**"Summary and description of invention"**

and insert therefor:

**--Summary--.**

On page 3, line 9, please insert:

**--Detailed Description--.**

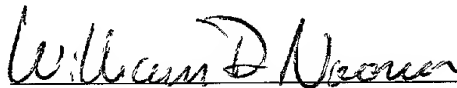
### **Conclusion**

If any minor matters remain to be addressed before examination of the application, the Examiner is invited to call the undersigned.

Respectfully submitted,

KLARQUIST SPARKMAN CAMPBELL  
LEIGH & WHINSTON, LLP

By



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**Marked-up Version of Amended Specification  
Pursuant to 37 C.F.R. §§ 1.121(b)-(c)**

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## METHODS FOR TREATING CELLS

### Priority Claim

5        This application claims priority under 35 U.S.C. § 119 to Great Britain  
Application No. 0013817.2, filed June 6, 2000.

### Field of the invention

10        This invention relates to methods for treating cells, e.g. proliferating cells, for  
example hyperproliferating cells, such as tumour cells, so as to damage them or reduce  
their proliferation.

### Background of the invention and prior art

15        Administration to mammals of cytokines is known as such, but is often poorly  
tolerated by the host (A Mire-Sluis, TIBTech Vol. 11 (1993); MS Moore, Ann Rev  
Immunol 9 (1991), 159-191).

20        It is also known to modify live virus vectors to carry genes encoding a cytokine or  
tumour antigen, see e.g. WO 96/26267 (Cantab Pharmaceuticals: Inglis et al) and  
references cited therein including WO 94/16716 (Virogenetics Corporation: Paoletti et  
al.).

25        Gene sequences of a large number of cytokine genes and other  
immunomodulatory proteins are known. For example, human GM-CSF and its gene are  
described in M Cantrell et al., Proc. Nat. Acad. Sci. 82 (1985), pp 6250-6254; F Lee et  
al., Proc. Nat. Acad. Sci. 82 (1985), pp 4360-4364 and G Wong et al., Science 228  
(1985), pp 810-815. The gene encoding murine GM-CSF is also known (Gough et al.,

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Virus vectors which are defective in respect of a gene essential for production of infectious virus, such that the virus can infect normal host cells and undergo replication and expression of viral antigen genes in such cells but cannot produce infectious virus are known and described in specification WO 92/05263 (Immunology Limited: Inglis et al) and WO 94/21807 (Cantab Pharmaceuticals Research Limited: Inglis et al).

WO 92/05263 (Immunology Limited: Inglis et al) particularly describes an HSV virus which is disabled by functional deletion of a gene encoding the essential glycoprotein (gH) which is required for virus infectivity.

It is also known to administer dendritic cell preparations to mammals. BM Colombo et al. (Immunology, 2000, 99 (1): 8-15) describes vaccination of mice with tumour extract-loaded dendritic cells and subsequent generation of a CD-4 antigen specific cell-mediated cytotoxic protective immune response.

It is also known that certain bacteria can possess anti-tumour activity. H Akaza et al. (Cancer, 1993, 72 (2): 558-563) describes the anti-tumour effects of Bacillus Calmette-Guerin (BCG) against urinary bladder cancer.

### **[Summary and description of the invention]**

#### **Summary**

According to an aspect of the invention there is provided a combination treatment for treating target cells, for example proliferating cells, e.g. hyperproliferating cells, e.g. tumour cells. The treatment comprises the steps of:

a) exposing target cells to a cell-damaging agent, for example, an agent which is capable of producing cell inflammation and/or lysis,

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b) exposing said target cells to a preparation of antigen-presenting cells, e.g. dendritic cells. The cell-damaging agent can contact the target cells, or can enter, or be taken up by them. This can enable the antigen-presenting cells to encounter substances such as antigens, that can be produced by exposure of the target cells to the cell-damaging agent  
5 in step a) of the process.

In alternative embodiments, step b) can precede step a) or be carried out at the same time as step a).

### **Detailed Description**

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The invention provides in one aspect a method of treating target cells to damage them and/or reduce their proliferation: the method comprises the steps of (a) exposing the target cells to a cell-damaging agent, and also (b) exposing said target cells to a preparation of antigen-presenting cells, thereby to damage said cells and/or reduce their  
15 proliferation. Step (b) can be carried out after step (a), e.g. at least about 30 minutes after step (a). The antigen-presenting cells can consist essentially of dendritic cells. The cell-damaging agent can consist essentially of a vector, e.g. a virus vector, for gene delivery. The damage produced by the agent can be indirect, e.g. by the immune response generated. Such a virus vector can comprise one or more gene sequences encoding an  
20 immunomodulatory protein and/or a tumour antigen, or a functional fragment thereof. The cell-damaging agent and the antigen-presenting cells can be delivered to target cells in vivo, or alternatively to in-vitro cells, in which case the treated target cells can then be implanted or administered into a subject.

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Thus in one form of embodiment, a method of treating cell proliferation in a subject can comprise administering to said subject separately or concurrently a preparation (a) which consists essentially of a cell-damaging agent, and a preparation (b) which consists essentially of an antigen-presenting cell preparation, in combination with a pharmaceutical excipient.